A marked-up version of the specification is provided to reflect the above changes.

In the "Brief Description of the Drawings":

~~FIG. 1 is a bar graph~~ FIGS. 1A and 1B are bar graphs showing the survival of dissociated sympathetic neurons grown in collagen gels after 2 or 6 day treatments, respectively, with NT-3 (2 ng/ml) or GDNF (50 ng/ml), in the presence or absence of OP-1.

In the claims:

For the convenience of the Examiner, all claims being examined, whether or not amended, are presented below.

Please cancel, without prejudice, claim 24.

1. (**Twice Amended**) A method for promoting survival or growth of mammalian neural cells, wherein said cells express an OP/BMP-activated serine/threonine kinase receptor and a GDNF/NGF-activated tyrosine kinase receptor, comprising:

contacting neural cells with an effective concentration of a preparation comprising

(a) an OP/BMP morphogen having an amino acid sequence having at least 70% homology with the C-terminal seven cysteine skeleton of human OP-1, wherein said OP/BMP morphogen can induce ectopic bone, and

(b) a GDNF/NGF neurotrophic factor selected from GDNF, BDNF, NT-3, NT-4, NT-5 and NT-6.

11. (**Amended**) A method as in claim 1, wherein said neural cells comprise neurons or neurological cells.

13. (**Amended**) A method as in claim 1, wherein said neural cells comprise peripheral nervous system cells.

15. (**Twice Amended**) A method as in claim 1, wherein said OP/BMP morphogen comprises an amino acid sequence having at least 80% homology with the C-terminal seven-

cysteine skeleton of human OP-1, and wherein said OP/BMP morphogen can induce ectopic bone.

16. (**Twice Amended**) A method as in claim 1, wherein said OP/BMP morphogen comprises an amino acid sequence having at least 90% homology with the C-terminal seven-cysteine skeleton of human OP-1, and wherein said OP/BMP morphogen can induce ectopic bone.

17. (**Twice Amended**) A method as in claim 1, wherein said OP/BMP morphogen comprises an amino acid sequence at least 70% identical to the C-terminal seven-cysteine skeleton of human OP-1.

18. (**Twice Amended**) A method as in claim 1, wherein said OP/BMP morphogen is selected from OP-1, OP-2, OP-3, BMP2, BMP3, BMP4, BMP5, BMP6 and BMP9.

19. (**Amended**) A method as in claim 1, wherein said effective concentration of the preparation is between 0.1 ng/ml and 10 μg/ml of said OP/BMP morphogen and between 0.1 ng/ml and 10 μg/ml of said GDNF/NGF neurotrophic factor.

20. (**Reiterated**) A method as in claim 19 wherein, said effective concentration is between 1 ng/ml and 100 ng/ml of said OP/BMP morphogen.

21. (**Reiterated**) A method as in claim 19, wherein said effective concentration is between 1 ng/ml and 100 ng/ml of said GDNF/NGF neurotrophic factor.

22. (**Reiterated**) A method as in claim 19, wherein said effective concentration is between 1 ng/ml and 100 ng/ml of said OP/BMP morphogen and between 1 ng/ml and 100 ng/ml of said GDNF/NGF neurotrophic factor.

23. (**Amended**) A method as in claim 1, wherein said GDNF/NGF neurotrophic factor comprises GDNF.

28. (**Twice Amended**) A pharmaceutical preparation for promoting the survival or growth of mammalian neural cells, wherein said cells express an OP/BMP-activated

serine/threonine kinase receptor and a GDNF/NGF-activated tyrosine kinase receptor, comprising:

(a) a GDNF/NGF neurotrophic factor selected from GDNF, BDNF, NT-3, NT-4, NT-5 and NT-6, and

(b) an OP/BMP morphogen having an amino acid sequence having at least 70% homology with the C-terminal seven cysteine skeleton of human OP-1, wherein said OP/BMP morphogen can induce ectopic bone.

29. (**Twice Amended**) A pharmaceutical preparation for inhibiting the death or degeneration of mammalian neural cells, wherein said cells express an OP/BMP-activated serine/threonine kinase receptor and a GDNF/NGF-activated tyrosine kinase receptor, comprising:

(a) a GDNF/NGF neurotrophic factor selected from GDNF, BDNF, NT-3, NT-4, NT-5 and NT-6, and

(b) an OP/BMP morphogen having an amino acid sequence having at least 70% homology with the C-terminal seven cysteine skeleton of human OP-1, wherein said OP/BMP morphogen can induce ectopic bone.

The claims presented above incorporate changes as indicated by the marked-up version below.

1. (**Twice Amended**) A method for promoting survival or growth of mammalian neural cells, wherein said cells express an OP/BMP-activated serine/<u>threonine</u> ~~theronine~~ kinase receptor and a GDNF/NGF-activated tyrosine kinase receptor, comprising:

contacting neural cells with <u>an effective concentration of</u> a preparation comprising

(a) an OP/BMP morphogen having an amino acid sequence ~~with~~ <u>having</u> at least 70% homology with the C-terminal seven cysteine skeleton of human OP-1<u>, wherein said OP/BMP morphogen can induce ectopic bone</u>, and

(b) a GDNF/NGF ~~neuroptrophic~~ <u>neurotrophic</u> factor <u>selected from GDNF, BDNF, NT-3, NT-4, NT-5 and NT-6</u>.

11. (**Amended**) A method as in claim 1, ~~any one of claims 1-4~~ wherein said neural cells comprise neurons or neurological cells.

13. (**Amended**) A method as in claim 1, ~~any one of claims 1-4~~ wherein said neural cells comprise peripheral nervous system cells.

15. (**Twice Amended**) A method as in claim 1, wherein said OP/BMP morphogen comprises an amino acid sequence having at least 80% homology with the C-terminal seven-cysteine skeleton ~~domain~~ of human OP-1, and wherein said OP/BMP morphogen can induce ectopic bone.

16. (**Twice Amended**) A method as in claim 1, wherein said OP/BMP morphogen comprises an amino acid sequence having at least 90% homology with ~~60% amino acid identity with~~ the C-terminal seven-cysteine skeleton ~~domain~~ of human OP-1, and wherein said OP/BMP morphogen can induce ectopic bone.

17. (**Twice Amended**) A method as in claim 1, wherein said OP/BMP morphogen comprises an amino acid sequence ~~having~~ at least 70% identical to ~~70% amino acid identity with~~ the C-terminal seven-cysteine skeleton ~~domain~~ of human OP-1.

18. (**Twice Amended**) A method as in claim 1, wherein said OP/BMP morphogen ~~comprises at least the C-terminal six- or seven-cysteine domain of a mammalian protein~~ is selected from ~~the group consisting of~~ OP-1, OP-2, OP-3, BMP2, BMP3, BMP4, BMP5, BMP6 and BMP9.

19. (**Amended**) A method as in claim 1, ~~any of claims 1-4~~ wherein said effective concentration of the preparation is between 0.1 ng/ml and 10 μg/ml of said OP/BMP morphogen and between 0.1 ng/ml and 10 μg/ml of said GDNF/NGF neurotrophic factor.

23. (**Amended**) A method as in claim 1, ~~any of claims 1-4~~ wherein said GDNF/NGF neurotrophic factor comprises ~~a mature, functional form of a protein selected from the group consisting of~~ GDNF ~~NGF, BDNF, NT-3, NT-4, NT-5 and NT-6~~.

28. **(Twice Amended)** A pharmaceutical preparation for promoting the survival or growth of mammalian neural cells, wherein said cells express an OP/BMP-activated serine/threonine ~~theronine~~ kinase receptor and a GDNF/NGF-activated tyrosine kinase receptor, comprising:

(a) a GDNF/NGF neurotrophic factor selected from GDNF, BDNF, NT-3, NT-4, NT-5 and NT-6, and

(b) an OP/BMP morphogen having an amino acid sequence having at least 70% homology with the C-terminal seven cysteine skeleton of human OP-1, wherein said OP/BMP morphogen can induce ectopic bone.

29. **(Twice Amended)** A pharmaceutical preparation for inhibiting the death or degeneration of mammalian neural cells, wherein said cells express an OP/BMP-activated serine/ threonine ~~theronine~~ kinase receptor and a GDNF/NGF-activated tyrosine kinase receptor, comprising:

(a) a GDNF/NGF neurotrophic factor selected from GDNF, BDNF, NT-3, NT-4, NT-5 and NT-6, and

(b) an OP/BMP morphogen having an amino acid sequence having at least 70% homology with the C-terminal seven cysteine skeleton of human OP-1, wherein said OP/BMP morphogen can induce ectopic bone.

REMARKS

The Office Communication mailed on July 29, 2002 indicates that the reply / amendment filed on May 2, 2002 (Paper No. 12) is not fully responsive to the Office Action mailed on October 23, 2001, because Applicants have failed to sign said amendment. Accordingly, Applicants submit this response, which combines the contents of the original unsigned reply / amendment of Paper No. 12, and the content of the signed Supplemental Amendment filed on May 3, 2002.

Claims 1-13 and 15-29 constitute the pending claims in the present application, and claims 1, 11, 13, 15-24, 28 and 29 are currently under consideration having been elected with traverse. Applicants will cancel non-elected claims upon the indication of allowable subject